WHAT IS CLAIMED IS:

1. A method for preparing monomeric cytotoxic drug/carrier conjugates with reduced low conjugated fraction (LCF) having the formula,

$Pr(-X-W)_m$

wherein:

Pr is a proteinaceous carrier,

X is a linker that comprises a product of any reactive group that can react with a proteinaceous carrier,

W is a cytotoxic drug ;

m is the average loading for a purified conjugation product such that the cytotoxic drug constitutes 7 - 9% of the conjugate by weight; and

$(-X-W)_m$ is a cytotoxic drug derivative,

said method comprising the steps of:

(1) adding the cytotoxic drug derivative to the proteinaceous carrier wherein the cytotoxic drug derivative is 4.5 - 11% by weight of the proteinaceous carrier;

(2) incubating the cytotoxic drug derivative and a proteinaceous carrier in a non-nucleophilic, protein-compatible, buffered solution having a pH in the range from about 7 to 9 to produce a monomeric cytotoxic drug/carrier conjugate, wherein the solution further comprises (a) an organic cosolvent, and (b) an additive comprising at least one C_6-C_{18} carboxylic acid or its salt, and wherein the incubation is conducted at a temperature ranging from about 30°C to about 35°C for a period of time ranging from about 15 minutes to 24 hours; and

(3) subjecting the conjugate produced in step (2) to a chromatographic separation process to separate monomeric cytotoxic drug derivative/ proteinaceous carrier conjugates with a loading in the range of 4 – 10 % by weight cytotoxic drug and with low conjugated fraction (LCF) below 10 percent from unconjugated proteinaceous carrier, cytotoxic drug derivative, and aggregated conjugates.

2. The method of claim 1, wherein the proteinaceous carrier is selected from a group consisting of hormones, growth factors, antibodies, antibody fragments, antibody mimics, and their genetically or enzymatically engineered counterparts.
3. The method of claim 1, wherein the proteinaceous carrier is an antibody.
4. The method of claim 3, wherein the antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, a Fab fragment and a F(ab)2 fragment.
5. The method of claim 4, wherein the humanized antibody is directed against the cell surface antigen CD22.
6. The method of claim 5, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody, and comprises a light chain variable region 5/44-gL1 (SEQ ID NO:19), and a heavy chain variable region 5/44-gH7 (SEQ ID NO:27).
7. The method of claim 5, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody comprising a light chain having a sequence set forth in SEQ ID NO: 28.
8. The method of claim 5, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody comprising a heavy chain having a sequence set forth in SEQ ID NO:30.
9. The method of claim 5, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody comprising a light chain having a sequence set forth in SEQ ID NO: 28 and a heavy chain having a sequence set forth in SEQ ID NO: 30.
10. The method of claim 5, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody that is a variant antibody obtained by an affinity maturation protocol and has increased specificity for human CD22.
11. The method of claim 1, wherein the cytotoxic drug is an inhibitor of tubulin polymerization.
12. The method of claim 1, wherein the cytotoxic drug is an alkylating agent that binds to and disrupts DNA.
13. The method of claim 1, wherein the cytotoxic drug inhibits protein synthesis.
14. The method of claim 1, wherein the cytotoxic drug is a tyrosine kinase inhibitor.

15. The method of claim 1, wherein the cytotoxic drug is selected from calicheamicins, thiotepa, taxanes, vincristine, daunorubicin, doxorubicin, epirubicin, esperamicins, actinomycin, authramycin, azaserines, bleomycins, tamoxifen, idarubicin, dolastatins/auristatins, hemiasterlins and maytansinoids.
16. The method of claim 1, wherein the cytotoxic drug is calicheamicin.
17. The method of claim 16, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.
18. The method of claim 1, wherein the cytotoxic drug is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.
19. The method of claim 1, wherein the linker is a hydrolyzable linker that is capable of releasing the cytotoxic drug from the conjugate after binding and entry into target cells.
20. The method of claim 19, wherein the hydrolyzable linker is 4-(4-acetylphenoxy) butanoic acid (AcBut).
21. The method of claim 1, wherein the additive of step (2) (b) is octanoic acid or its salt.
22. The method of claim 1, wherein the additive of step (2) (b) is decanoic acid or its salt.
23. The method of claim 1, wherein the chromatographic separation process of step (3) is size exclusion chromatography (SEC).
24. The method of claim 1, wherein the chromatographic separation process of step (3) is HPLC, FPLC or Sephacryl S-200 chromatography.
25. The method of claim 1, wherein the chromatographic separation process of step (3) is hydrophobic interaction chromatography (HIC).
26. The method of claim 25, wherein the hydrophobic interaction chromatography (HIC) is carried out using Phenyl Sepharose 6 Fast Flow chromatographic medium, Butyl Sepharose 4 Fast Flow chromatographic medium, Octyl Sepharose 4 Fast Flow chromatographic medium, Toyopearl Ether-650M chromatographic medium, Macro-Prep methyl HIC medium or Macro-Prep t-Butyl HIC medium.
27. The method of claim 25, wherein the hydrophobic interaction chromatography (HIC) is carried out using Butyl Sepharose 4 Fast Flow chromatographic medium.

28. A monomeric cytotoxic drug derivative/carrier conjugate produced by the method of claim 1.

29. The monomeric cytotoxic drug derivative/carrier of claim 28, wherein the cytotoxic drug is calicheamicin.

30. The monomeric cytotoxic drug derivative/carrier conjugate of claim 28, wherein the carrier is an antibody.

31. The monomeric cytotoxic drug derivative/carrier conjugate of claim 30, wherein the antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, a Fab fragment and a F(ab)2 fragment.

32. The monomeric cytotoxic drug derivative/carrier conjugate of claim 31, wherein the humanized antibody is directed against the cell surface antigen, CD22.

33. The monomeric cytotoxic drug derivative/carrier conjugate of claim 32, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody, and comprises a light chain variable region 5/44-gL1 (SEQ ID NO:19), and a heavy chain variable region 5/44-gH7 (SEQ ID NO:27).

34. The monomeric cytotoxic drug derivative/carrier conjugate of claim 32, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody comprising a light chain having a sequence set forth in SEQ ID NO: 28.

35. The monomeric cytotoxic drug derivative/carrier conjugate of claim 32, wherein the humanized anti-CD22 antibody is a CDR-grafted comprising a heavy chain having a sequence set forth in SEQ ID NO:30.

36. The monomeric cytotoxic drug derivative/carrier conjugate of claim 32, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody comprising a light chain having a sequence set forth in SEQ ID NO: 28 and a heavy chain having a sequence set forth in SEQ ID NO: 30.

37. The monomeric cytotoxic drug derivative/carrier conjugate of claim 32, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody that is a variant antibody obtained by an affinity maturation protocol and has increased specificity for human CD22.

38. The monomeric cytotoxic drug derivative/carrier conjugate of claim 32, wherein the cytotoxic drug derivative is calicheamicin.

39. The monomeric cytotoxic drug derivative/carrier conjugate of claim 38, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.

40. The monomeric cytotoxic drug derivative/carrier conjugate of claim 38 or 39, wherein the calicheamicin derivative is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.

41. The monomeric cytotoxic drug derivative/carrier of claim 38, wherein the linker is a hydrolyzable linker that is capable of releasing the cytotoxic drug from the conjugate after binding and entry into target cells.

42. The monomeric cytotoxic drug derivative/carrier conjugate of claim 41, wherein the hydrolyzable linker is 4-(4-acetylphenoxy) butanoic acid (AcBut).

43. A monomeric calicheamicin derivative/anti-CD22 antibody conjugate having the formula,

$Pr(-X-S-S-W)_m$

wherein:

Pr is an anti-CD22 antibody;

X is a hydrolyzable linker that comprises a product of any reactive group that can react with an antibody;

W is a calicheamicin radical;

m is the average loading for a purified conjugation product such that the calicheamicin constitutes 4 – 10% of the conjugate by weight; and

$(-X-S-S-W)_m$ is a calicheamicin derivative.

44. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 43, wherein the antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, a Fab fragment and a F(ab)2 fragment.

45. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 44, wherein the anti-CD22 antibody has specificity for human CD22 and comprises a heavy chain wherein the variable domain comprises a CDR having at least one of the sequences given as H1 in Figure 1 (SEQ ID NO:1) for CDR-H1, as H2 in Figure 1 (SEQ ID NO:2) or H2' (SEQ ID NO:13) or H2" (SEQ ID NO:15) or H2"' (SEQ ID NO:16) for CDR-H2, or as H3 in Figure 1 (SEQ ID NO:3) for CDR-H3, and comprises a light chain wherein the variable

domain comprises a CDR having at least one of the sequences given as L1 in Figure 1 (SEQ ID NO:4) for CDR-L1, as L2 in Figure 1 (SEQ ID NO:5) for CDR-L2, or as L3 in Figure 1 (SEQ ID NO:6) for CDR-L3.

46. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 44, wherein the antibody comprises a heavy chain wherein the variable domain comprises a CDR having at least one of the sequences given in SEQ ID NO:1 for CDR-H1, SEQ ID NO:2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 for CDR-H2, or SEQ ID NO:3 for CDR-H3, and a light chain wherein the variable domain comprises a CDR having at least one of the sequences given in SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2, or SEQ ID NO:6 for CDR-L3.

47. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 44, wherein the antibody molecule comprises SEQ ID NO:1 for CDR-H1, SEQ ID NO: 2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 for CDR-H2, SEQ ID NO:3 for CDR-H3, SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2 and SEQ ID NO:6 for CDR-L3.

48. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 44, wherein the humanized antibody is a CDR-grafted anti-CD22 antibody.

49. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.

50. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 49, wherein the human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on a human sub-group I consensus sequence and comprise non-human donor residues at positions 1, 28, 48, 71 and 93.

51. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 50, wherein the antibody further comprises non-human donor residues at positions 67 and 69.

52. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the CDR-grafted antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on a

human sub-group I consensus sequence and further comprising non-human donor residues at positions 2, 4, 37, 38, 45 and 60.

53. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 52, wherein the CDR-grafted antibody further comprises a non-human donor residue at position 3.

54. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the CDR-grafted antibody comprises a light chain variable region 5/44-gL1 (SEQ ID NO:19) and a heavy chain variable region 5/44-gH7 (SEQ ID NO:27).

55. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the CDR-grafted antibody comprises a light chain having the sequence as set forth in SEQ ID NO: 28.

56. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the CDR-grafted antibody comprises a heavy chain having the sequence as set forth in SEQ ID NO:30.

57. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the CDR-grafted antibody comprises a light chain having the sequence as set forth in SEQ ID NO: 28 and a heavy chain having the sequence as set forth in SEQ ID NO: 30.

58. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 48, wherein the CDR-grafted antibody is a variant antibody obtained by an affinity maturation protocol and has increased specificity for human CD22.

59. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 44, wherein the anti-CD22 antibody is a chimeric antibody comprising the sequences of the light and heavy chain variable domains of the monoclonal antibody set forth in SEQ ID NO:7 and SEQ ID NO:8 respectively.

60. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 44, wherein the anti-CD22 antibody comprises a hybrid CDR comprising a truncated donor CDR sequence wherein the missing portion of the donor CDR is replaced by a different sequence and forms a functional CDR.

61. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 43, wherein the calicheamicin derivative is a gamma calicheamicin or a N-acetyl gamma calicheamicin derivative.

62. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 61, wherein the calicheamicin derivative is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.

63. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 43, wherein the hydrolyzable linker is a bifunctional linker that is capable of releasing the calicheamicin derivative from the conjugate after binding and entry into target cells.

64. The monomeric calicheamicin derivative/anti-CD22 antibody conjugate of claim 63, wherein the bifunctional linker is 4-(4-acetylphenoxy) butanoic acid (AcBut).

65. A method for the preparation of a stable lyophilized composition of a monomeric cytotoxic drug derivative/carrier conjugate, the method comprising:

(a) dissolving the monomeric cytotoxic drug derivative/carrier conjugate to a final concentration of 0.5 to 2 mg/mL in a solution comprising a cryoprotectant at a concentration of 1.5%-5% by weight, a polymeric bulking agent at a concentration of 0.5-1.5% by weight, electrolytes at a concentration of 0.01M to 0.1 M, a solubility facilitating agent at a concentration of 0.005-0.05% by weight, buffering agent at a concentration of 5-50 mM such that the final pH of the solution is 7.8-8.2, and water;

(b) dispensing the above solution into vials at a temperature of +5 °C to +10 °C;

(c) freezing the solution at a freezing temperature of -35 °C to –50 °C;

(d) subjecting the frozen solution to an initial freeze drying step at a primary drying pressure of 20 to 80 microns at a shelf-temperature at –10 °C to –40 °C for 24 to 78 hours; and

(e) subjecting the freeze-dried product of step (d) to a secondary drying step at a drying pressure of 20 to 80 microns at a shelf temperature of +10°C to + 35°C for 15 to 30 hours.

66. The method of claim 65, wherein the cytotoxic drug derivative is an inhibitor of tubulin polymerization.

67. The method of claim 65, wherein the cytotoxic drug derivative is an alkylating agent that binds to and disrupt DNA.

68. The method of claim 65, wherein the cytotoxic drug derivative is an inhibitor of protein synthesis.

69. The method of claim 65, wherein the cytotoxic drug derivative is a tyrosine kinase inhibitor.

70. The method of claim 65, wherein the cytotoxic drug derivative is selected from calicheamicins, thiotepa, taxanes, vincristine, daunorubicin, doxorubicin, epirubicin, actinomycin, authramycin, azaserines, bleomycins, tamoxifen, idarubicin, dolastatins/auristatins, hemiasterlins, and maytansinoids.

71. The method of claim 65, wherein the cytotoxic drug derivative is calicheamicin.

72. The method of claim 65, wherein the cytotoxic drug derivative is gamma calicheamicin or N-acetyl calicheamicin.

73. The method of claim 65, further optionally comprising a bioactive agent at a therapeutically effective concentration.

74. The method of claim 73, wherein the bioactive agent is a cytotoxic drug.

75. The method of claim 73, wherein the bioactive agent is a growth factor.

76. The method of claim 73, wherein the bioactive agent is a hormone.

77. The method of claim 73, wherein the cryoprotectant is selected from a group comprising alditol, mannitol, sorbitol, inositol, polyethylene glycol, aldonic acid, uronic acid, aldaric acid, aldoses, ketoses, amino sugars, alditols, inositols, glyceraldehydes, arabinose, lyxose, pentose, ribose, xylose, galactose, glucose, hexose, idose, mannose, talose, heptose, glucose, fructose, gluconic acid, sorbitol, lactose, mannitol, methyl α-glucopyranoside, maltose, isoascorbic acid, ascorbic acid, lactone, sorbose, glucaric acid, erythrose, threose, arabinose, allose, altrose, gulose, idose, talose, erythrulose, ribulose, xylulose, psicose, tagatose, glucuronic acid, gluconic acid, glucaric acid, galacturonic acid, mannuronic acid, glucosamine, galactosamine, sucrose, trehalose, neuraminic acid, arabinans, fructans, fucans, galactans, galacturonans, glucans, mannans, xylans, levan, fucoidan,

carrageenan, galactocarolose, pectins, pectic acids, amylose, pullulan, glycogen, amylopectin, cellulose, dextran, pustulan, chitin, agarose, keratin, chondroitin, dermatan, hyaluronic acid, alginic acid, xanthan gum, starch, sucrose, glucose, lactose, trehalose, ethylene glycol, polyethylene glycol, polypropylene glycol, glycerol, and pentaerythritol.

78. The method of claim 65, wherein the cryoprotectant is sucrose.

79. The method of claim 78, wherein the sucrose is present at a concentration of 1.5% by weight.

80. The method of claim 65, wherein the polymeric bulking agent is Dextran 40, and is at a concentration of 0.9% by weight.

81. The method of claim 65, wherein the polymeric bulking agent is hydroxyethyl starch 40, and is at a concentration of 0.9% by weight.

82. The method of claim 65, wherein the electrolyte is sodium chloride, and is present at a concentration of 0.05 M.

83. The method of claim 65, wherein the solubility facilitating agent is a surfactant.

84. The method of claim 83, wherein the surfactant is polysorbate 80, and is present at a concentration of 0.01% by weight.

85. The method of claim 65, wherein the buffering agent is tromethamine, and is present at a concentration of 0.02 M.

86. The method of claim 65, wherein the pH of the solution of step (a) is 8.0.

87. The method of claim 65, wherein the solution in step (b) is dispensed into vials at a temperature of +5 °C.

88. The method of claim 65, wherein in step (c) the freezing of the solution in the vials is carried out at a freezing temperature of -45 °C.

89. The method of claim 65, wherein in step (d) the frozen solution is subjected to an initial freeze drying step at a primary drying pressure of 60 microns and at a shelf temperature of –30 °C for 60 hours.

90. The method of claim 65, wherein in step (e), the freeze-dried product of step (d) is subjected to a secondary drying step at a drying pressure of 60 microns at a shelf temperature of +25°C for 24 hours.

91. A composition comprising a therapeutically effective dose of a monomeric cytotoxic drug derivative/carrier conjugate prepared by the method of claim 65.

92. The composition of claim 91, wherein the carrier in the monomeric cytotoxic drug derivative/carrier conjugate is a proteinaceous carrier.

93. The composition of claim 92, wherein the proteinaceous carrier is selected from a group consisting of hormones, growth factors, antibodies, and antibody mimics.

94. The composition of claim 93, wherein the antibody is a human monoclonal antibody.

95. The composition of claim 93, wherein the antibody is a chimeric antibody.

96. The composition of claim 93, wherein the antibody is a human antibody.

97. The composition of claim 93, wherein the antibody is a humanized antibody.

98. The composition of claim 97, wherein the humanized antibody is directed against the cell surface antigen CD22.

99. The composition of claim 98, wherein the anti-CD22 antibody has specificity for human CD22, and comprises a heavy chain wherein the variable domain comprises a CDR having at least one of the sequences given as H1 in Figure 1 (SEQ ID NO:1) for CDR-H1, as H2 in Figure 1 (SEQ ID NO:2), or H2' (SEQ ID NO:13), or H2" (SEQ ID NO:15), or H2"' (SEQ ID NO:16) for CDR-H2, or as H3 in Figure 1 (SEQ ID NO:3) for CDR-H3, and comprises a light chain wherein the variable domain comprises a CDR having at least one of the sequences given as L1 in Figure 1 (SEQ ID NO:4) for CDR-L1, as L2 in Figure 1 (SEQ ID NO:5) for CDR-L2, or as L3 in Figure 1 (SEQ ID NO:6) for CDR-L3.

100. The composition of claim 98, wherein the antibody comprises a heavy chain wherein the variable domain comprises a CDR having at least one of the sequences given in SEQ ID NO:1 for CDR-H1, SEQ ID NO:2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 for CDR-H2, or SEQ ID NO:3 for CDR-H3, and a light chain wherein the variable domain comprises a CDR having at least one of the sequences given in SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2, or SEQ ID NO:6 for CDR-L3.

101. The composition of claim 98, wherein the antibody comprises SEQ ID NO:1 for CDR-H1, SEQ ID NO: 2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 for CDR-H2, SEQ ID NO:3 for CDR-H3, SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2, and SEQ ID NO:6 for CDR-L3.
102. The composition of claim 98, wherein the humanized anti-CD22 antibody is a CDR-grafted humanized anti-CD22 antibody and comprises a light chain variable region 5/44-gL1 (SEQ ID NO:19), and a heavy chain variable region 5/44-gH7 (SEQ ID NO:27).
103. The composition of claim 98, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody having specificity for human CD22 and comprises a light chain having a sequence set forth in SEQ ID NO: 28.
104. The composition of claim 98, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody having specificity for human CD22 and comprises a heavy chain having a sequence set forth in SEQ ID NO:30.
105. The composition of claim 98, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody having specificity for human CD22 and comprises a light chain having a sequence set forth in SEQ ID NO: 28 and a heavy chain having a sequence set forth in SEQ ID NO: 30.
106. The composition of claim 98, wherein the humanized anti-CD22 antibody is a CDR-grafted antibody that is a variant antibody having increased specificity for human CD22, wherein the variant antibody is obtained by an affinity maturation protocol.
107. The composition of claim 91, wherein the cytotoxic drug is calicheamicin.
108. The composition of claim 107, wherein the calicheamicin is gamma calicheamicin or N-acetyl calicheamicin.
109. The composition of claim 91, further optionally comprising a bioactive agent.
110. The composition of claim 109, wherein the bioactive agent is a cytotoxic drug.
111. The composition of claim 109, wherein the bioactive agent is a growth factor.
112. The composition of claim 109, wherein the bioactive agent is a hormone.
113. A method of treating a subject with a proliferative disorder, the method comprising administering a therapeutically effective dose of the composition of claim 91.

114. The method of treatment of claim 113, wherein the therapeutically effective dose of the composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially, intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, entereally, intravaginally, sublingually or rectally.

115. The method of treatment of claim 113, wherein the therapeutically effective dose of the composition of the invention is administered intravenously.

116. The method of claim 113, wherein the subject is a human subject and the proliferative disorder is cancer.

117. The method of claim 116, wherein the cancer is a B-cell malignancy.

118. The method of claim 117, wherein the B-cell malignancy is leukemia.

119. The method of claim 118, wherein the leukemia expresses cell surface antigen CD22.

120. The method of claim 117, wherein the B-cell malignancy is lymphoma.

121. The method of claim 120, wherein the lymphoma expresses cell surface antigen CD22.

122. The method of claim 116, wherein the cancer is a carcinoma.

123. The method of claim 116, wherein the cancer is a sarcoma.

124. A method of treating a B-cell malignancy, the method comprising administering to a patient in need of said treatment a therapeutically effective composition comprising a cytotoxic drug-anti-CD22-antibody conjugate.

125. The method of claim 124, wherein the B-cell malignancy is a lymphoma.

126. The method of claim 125, wherein the B-cell malignancy is a Non-Hodgkin's lymphoma.

127. The method of claim 124, comprising administering the therapeutically effective composition of the cytotoxic drug-anti-CD22-antibody conjugate with one or more bioactive agents.

128. The method of claim 124, wherein the cytotoxic drug in the cytotoxic drug conjugate anti-CD22 is selected from the group consisting of calicheamicins, thiotepa, taxanes, vincristine, daunorubicin, doxorubicin, epirubicin, actinomycin, authramycin, azaserines, bleomycins, tamoxifen, idarubicin, dolastatins/auristatins, hemiasterlins, maytansinoids, and esperamicins.

129. The method of claim 124, wherein the cytotoxic drug is calicheamicin.

130. The method of claim 126, wherein the calicheamicin is gamma calicheamicin or N-acetyl calicheamicin.

131. The method of claim 127, wherein the one or more bioactive agents are selected from a group consisting of antibodies, growth factors, hormones, cytokines, anti-hormones, xanthines, interleukins, interferons, and cytotoxic drugs.

132. The method of claim 131, wherein the bioactive agent is an antibody.

133. The method of claim 132, wherein the antibody is directed against a cell surface antigen expressed on B-cell malignancies.

134. The method of claim 133, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

135. The method of claim 134, wherein the anti-CD20 antibody is rituximab.

136. The method of claim 131, wherein the cytokines or growth factors are selected from a group consisting of interleukin 2 (IL-2), TNF, CSF, GM-CSF, and G-CSF.

137. The method of claim 131, wherein the hormone is a steroid hormone and is selected from estrogens, androgens, progestins, and corticosteroids.

138. The method of claim 131, wherein the cytotoxic drug is selected from the group consisting of doxorubicin, daunorubicin, idarubicin, aclarubicin, zorubicin, mitoxantrone, epirubicin, carubicin, nogalamycin, menogaril, pitarubicin, valrubicin, cytarabine, gemcitabine, trifluridine, ancitabine, enocitabine, azacitidine, doxifluridine, pentostatin, broxuridine, capecitabine, cladribine, decitabine, floxuridine, fludarabine, gougerotin, puromycin, tegafur, tiazofurin, adriamycin, cisplatin, carboplatin, cyclophosphamide, dacarbazine, vinblastine, vincristine, mitoxantrone, bleomycin, mechlorethamine, prednisone, procarbazine methotrexate, flurouracils, etoposide, taxol, taxol analogs, and mitomycin.

139. The method of claim 131, wherein the therapeutically effective composition of the cytotoxic drug-anti-CD22-antibody conjugate is administered together with one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

C. COP (cyclophosphamide, vincristine, and prednisone);

D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin;

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin, and leucovorin);

I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD(adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P. DHAP (dexamethasone, high-dose cytaribine, and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

140. The method of claim 131, wherein the therapeutically effective composition of the cytotoxic drug-anti-CD22-antibody conjugate is administered prior to the administration of one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

C. COP (cyclophosphamide, vincristine, and prednisone);

D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin and vincristine);

H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);

I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K. MOPP alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P. DHAP (dexamethasone, high-dose cytaribine, and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone)

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

141. The method of claim 131, wherein the therapeutically effective composition of the cytotoxic drug-anti-CD22-antibody conjugate is administered subsequent

to the administration of one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of bioactive agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);
B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);
C. COP (cyclophosphamide, vincristine, and prednisone);
D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);
E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin;
F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);
G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);
H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);
I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);
J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine), alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);
L. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);
N. IMVP-16 (ifosfamide, methotrexate, and etoposide);
O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);
P. DHAP (dexamethasone, high-dose cytaribine, and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone)

142. The method of claim 131, wherein the therapeutically effective composition of the cytotoxic drug-anti-CD22-antibody conjugate is administered together with an antibody directed against a cell surface antigen on B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

C. COP (cyclophosphamide, vincristine, and prednisone);

D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);

I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

143. A method of treating aggressive lymphomas comprising administering to a patient in need of said treatment a therapeutically effective composition of a monomeric calicheamicin derivative-anti-CD22-antibody conjugate together with one or more bioactive agents.

144. The method of claim 143, wherein the monomeric calicheamicin derivative-anti-CD22 antibody conjugate is CMC-544.